

Attn: Dkt PXE-006.US
9400-0006
PATENT

Sector 8 ✓

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on Dec. 19, 2000.

12/19/00

Date

Gail Wardwell

Signature



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

FRANCIS et al.

Serial No.: 09/657,289

Group Art Unit: 1645

Filing Date: September 7, 2000

Examiner: Unassigned

Title: LUCIFERASE EXPRESSION CASSETTES AND METHODS OF USE

TRANSMITTAL LETTER

Assistant Commissioner for Patents
Box Missing Part
Washington, D.C. 20231

Sir:

This is in response to the Notice to File Missing Parts dated October 20, 2000.

Transmitted herewith for filing are the following documents: a copy of the Notice to File Missing Parts; Declaration for Utility or Design Patent Application signed by the inventors; Power of Attorney or Authorization of Agent, Not Accompanying Application; copy of executed assignment; Blanket Petition for Extension of Time and Authorization to Charge or Credit Deposit Account; and Request for Corrected Filing Receipt with a copy of the Filing Receipt with changes highlighted. Also enclosed is a check in the amount of \$2524 (surcharge, \$130; statutory basic filing fee; \$690; additional claim fees, \$1704) to cover the fees required.

The Commissioner is hereby authorized to charge any additional fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648.

Respectfully submitted,

Date: 19 Dec 2000

By: Gary R. Fabian

Gary R. Fabian
Registration No. 33,875
Agent for Applicants

Customer No. 26789
ROBINS & ASSOCIATES
90 Middlefield Road, Suite 200
Menlo Park, CA 94025
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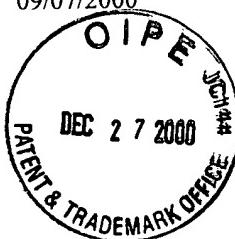


UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. 20231
www.uspto.gov

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
09/657,289	09/07/2000	Kevin P Francis	9400-0006

Charles K Sholtz
Xenogen Corporation
860 Atlantic Avenue
Alameda, CA 94501



FORMALITIES LETTER



OC000000005491159

Date Mailed: 10/20/2000

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given TWO MONTHS from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee is missing.
Applicant must submit \$ 690 to complete the basic filing fee and/or file a small entity statement claiming such status (37 CFR 1.27).
- Total additional claim fee(s) for this application is \$1704.
 - \$846 for 47 total claims over 20.
 - \$858 for 11 independent claims over 3.
- The oath or declaration is unsigned.
- To avoid abandonment, a late filing fee or oath or declaration surcharge as set forth in 37 CFR 1.16(e) of \$130 for a non-small entity, must be submitted with the missing items identified in this letter.

- **The balance due by applicant is \$ 2524.**

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A copy of this notice MUST be returned with the reply.

K. Sholtz
Customer Service Center
Initial Patent Examination Division (703) 308-1202
PART 2 - COPY TO BE RETURNED WITH RESPONSE

Atty Dkt # -006.US

9400-0006

PATENT

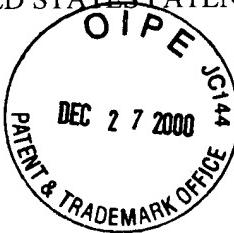
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Dec. 19, 2000

12/19/00
Date

Gail Wardwell
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In Re Application of:

FRANCIS et al.

Serial No.: 09/657,289

Group Art Unit: 1645

Filing Date: September 7, 2000

Examiner: Unassigned

Title: LUCIFERASE EXPRESSION CASSETTES AND METHODS OF USE

REQUEST FOR A CORRECTED FILING RECEIPT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please furnish the undersigned with a corrected filing receipt for the above-identified application. The corrections needed are as follows:

Under **TITLE** please replace:

"Mehtods" with --Methods--

Attached is a copy of the Filing Receipt with the correction highlighted. Also included is a copy of the Application Transmittal Letter and page 1 of the Application showing the correct spelling.

It is believed that no fee is due. If for any reason a fee is found to be necessary, our Deposit Account No. 18-1648 may be charged therefor.

Respectfully submitted,

Date: 19 Dec 2000

By:

Gary R. Fabian
Gary R. Fabian
Registration No. 33,875
Agent for Applicants

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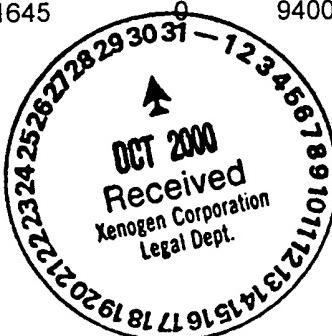
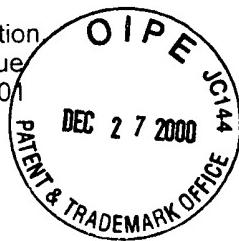


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APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
09/657,289	09/07/2000	1645	0	9400-0006	4	67	14

Charles K Sholtz
 Xenogen Corporation
 860 Atlantic Avenue
 Alameda, CA 94501



FILING RECEIPT



OC00000005491158

Date Mailed: 10/20/2000

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the PTO processes the reply to the Notice, the PTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s)

Kevin P Francis, Alameda, CA ;
 Pamela R Contag, San Jose, CA ;
 Danny J Joh, Fremont, CA ;

Continuing Data as Claimed by Applicant

THIS APPLN CLAIMS BENEFIT OF 60/152,904 09/08/1999

Foreign Applications

If Required, Foreign Filing License Granted 10/20/2000

Title

Methods

Luciferase expression cassettes and methods of use

Preliminary Class

435

Data entry by : WASHINGTON, KAREN

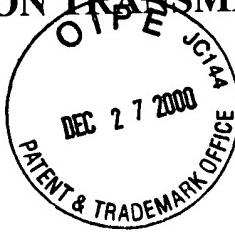
Team : OIPE

Date: 10/20/2000



APPLICATION TRANSMITTAL LETTER

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231



Sir:

- "Express Mail" Mailing Label No. EL 457 531 262 US, Date of Deposit September 7, 2000. I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Patricia K. Hinman
(Typed or Printed Name of Person Mailing Paper or Fee)

Patricia K. Hinman
(Signature of Person Mailing Paper or Fee)

Transmitted herewith for filing is the patent application of Kevin P. FRANCIS, Pamela R. CONTAG, and Danny J. JOH for LUCIFERASE EXPRESSION CASSETTES AND METHODS OF USE.

Enclosed are:

- 4 sheets of drawings.
 A claim for foreign priority under 35 U.S.C. § 119/363 in
— a separate document — the declaration.
 A claim for priority under 35 U.S.C. § 119(e)(1) in
— a separate document X the declaration.
 A certified copy of the priority document.
 Verified Statement(s) Claiming Small Entity Status.
 Other: Statement to Support Filing and Submission in Accordance with 37 C.F.R. §§ 1.821-1.825; return receipt postcard.

The declaration of the inventor X is enclosed X unsigned.

LUCIFERASE EXPRESSION CASSETTES AND METHODS OF USE

TECHNICAL FIELD

The present invention relates to luciferase expression vectors, methods of making
5 same and methods of use thereof.

BACKGROUND OF THE INVENTION

Bioluminescent bacteria are widely found in both marine and terrestrial environments. Interestingly, all identified species of naturally occurring marine and terrestrial bioluminescent
10 bacteria are Gram-negative. To date, at least eleven species in four Gram-negative genera have been described: *Vibrio*, *Photobacterium*, *Shewanella* (*Altermonas*) and *Photorhabdus* (*Xenorhabdus*). In all these species, the five genes responsible for bioluminescence are clustered in the *lux* operon (*luxCDABE*).

The bioluminescence (emitted blue-green light having a wavelength of about 490 nm) is thought to result from a luciferase-catalyzed oxidation of reduced flavin mononucleotide (FMNH₂) and a long-chain fatty aldehyde. The luciferase enzyme is encoded by two subunits (*luxAB*), whereas the fatty acid reductase polypeptides responsible for the biosynthesis of the aldehyde substrate for the luminescent reaction are encoded by the three genes *luxCDE*. The genes encoding luciferase and the fatty acid reductase polypeptides have been cloned from the
20 *lux* operons of *Vibrio*, *Photobacterium* and *Photorhabdus* and sequenced. In each case, the *luxCDE* genes flank the *luxAB* genes, with transcription in the order *luxCDABE*. Although a number of additional *lux* genes have been identified in each of these three bacteria, only *luxA-E* are essential for the biosynthesis of light (reviewed by Meighen, E., (1993), *The FASEB Journal* 7:1016-1022 and Ulitzur, S., (1997), *J. Biolumin Chemilumin* 12:179-192).

25 Methods described in U.S. Patent 5,650,135, make possible the detection of bioluminescent bacteria in a living animal without dissecting or otherwise opening the animal up ("in vivo monitoring") – the light is detected through muscle, skin, fur & other traditionally "opaque" tissues using a highly sensitive camera. In this context and others, it would therefore be desirable to confer bioluminescence properties on a bacterium of one's choice, so that the
30 bacterium could be followed with *in vivo* monitoring in various models of infection. In particular, it would be desirable to confer such bioluminescence properties on Gram-positive